MRI Longitudinal Study of Dementia Analysis

INF2178: Experimental Design for Data Science

Instructor: Professor Shion Guha

Yuanyuan Pan 1003980150

Assignment Introduction

This assignment aims to investigate the longitudinal change in normalized whole brain volume (nWBV) among subjects diagnosed with/without dementia, mainly focusing on the influence of gender and dementia status over a series of visits. The data were obtained from MRI scans conducted on subjects aged 60 to 96.

Motivated by the interest to understand the progression of dementia and potential factors influencing brain volume alterations, this study seeks to explore whether differences in brain volume alterations exist between gender and among different dementia status groups across several visits. By considering the span of visit times as a within-subject factor and gender and dementia status as between-subject factors, the study employs statistical techniques, including the exploratory data analysis (EDA) and mixed-effect ANOVA to gain insights into how gender and dementia status affect the trajectory of nWBV changes over multiple visits.

The study addresses two fundamental research questions:

1. How do gender influence the longitudinal changes in normalized brain volume over multiple visits?
2. How do dementia status influence the longitudinal changes in normalized brain volume over multiple visits?

Data Pre-processing and Cleaning

In the data pre-processing step, the data named “INF2178_A4_data.csv” has been read into the data frame for analysis. This dataset is a subset of data from a longitudinal study on MRI results, originally found from Kaggle. It contains sixteen variables, nevertheless, only five variables have been kept for this study, that is, subject ID, group, visit, gender, and nWBV. In the data cleaning process, the values of the variable “visit” have changed to categorical, mapping the numerical times of visit to first, second, etc. Moreover, the original variable name for gender is “M/F”, and it has been changed to “gender” for better understanding.

Exploratory Data Analysis

Summary statistics tables of nWBV:

Table 1

Visit	Group	Mean	Median	Standard deviation
First	Converted Demented Nondemented	0.74 0.72 0.75	0.73 0.73 0.75	0.03 0.03 0.04
Second	Converted Demented Nondemented	0.73 0.71 0.74	0.72 0.71 0.74	0.04 0.03 0.04

Above table records the summary statistics of nWBN, categorized by different dementia status groups and visits. By examining the statistics, the nWBV tends to slightly decrease from the first to second visit in general, indicating a decrease in brian health. Among all the groups, demented subjects tend to have a relatively more pronounced decreasing trend. However, it seems that there is no obvious difference in nWBV across different groups. By standard deviation, the spread of nWBV values within each group shows a small variability.

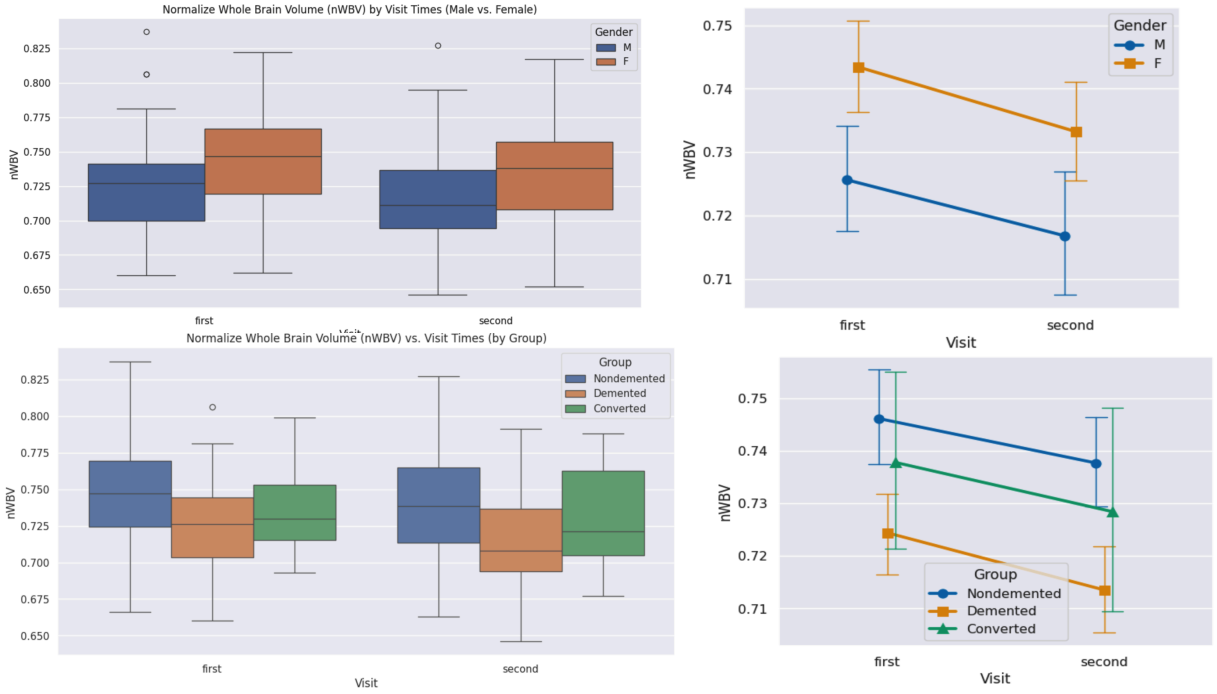
Table 2

Visit	Gender	Mean	Median	Standard deviation
First	Female Male	0.74 0.73	0.75 0.73	0.04 0.04

Second	Female Male	0.73 0.72	0.74 0.71	0.04 0.04

Above table records the statistics of nWBN, categorized by gender and visits. By examining the statistics, the nWBV tends to slightly decrease from the first to second visit regardless of the gender, also indicating a decrease in brian health. In general, females tend to have a higher value in nWBN compared to males, nevertheless, no obvious difference is detected in nWBV across different genders. The standard deviation remained the same, meaning the spread of nWBV values within each gender group have similar variability.

Box plots vs. Point plots:



The above **upper pair** of box plot and point plot is the nWBV by different genders across visit times. By examining the box plot and the trend on the point plot, regardless of the gender, there is a clear decline on nWBV from first to second visit. Female subjects tend to have a higher nWBV than male in general, indicating a better brian function health; outliers with higher nWBV exist in male subjects, which means nWBV distribution in male subjects have a relatively larger variability. The spread of the middle 50% data seems to be identical regardless of the gender and visit times. The nWBV of Female subjects are normally distributed while male subjects are slightly right skewed.

The above **lower pair** of box plot and point plot is the nWBV by different dementia status groups across visit times. By examining the box plot and the trend on the point plot, regardless of the group, there is also a clear decline on nWBV from first to second visit, indicating a decrease in brain health. Focusing on the point plot, the converted group tends to have a larger confidence interval, indicating a higher level of uncertainty and variability in the estimated parameter. According to the boxplot, the middle 50% data did not have obvious change for the nondemented and demented group from first to the second visit, however, the converted group shows a pronounced increase in its middle 50% data spread. Moreover, the lower the nWBV, the higher the chance a subject is diagnosed with dementia.

Mixed-Effect ANOVA

According to what has been specified in research questions, the following mixed-effect ANCOVAs (two-way) will focus on examining whether there are significant differences in nWBV across different visits (within-subject factor), taking into account the between-subject factors of gender and dementia status groups. In the following ANOVAs, the independent variables are visit and gender/dementia status group, the dependent variable is nWBV.

1. nWBV vs. Visit by Gender ANOVA:

Null Hypothesis (H0):
There is no significant difference in mean nWBV across different visits.
There is no significant difference in mean nWBV between different genders.
There is no significant interaction effect between visits and gender on mean nWBV.
Alternative Hypothesis (H1):
There is a significant difference in mean nWBV across different visits.
There is a significant difference in mean nWBV between different genders.
There is a significant interaction effect between visits and gender on mean nWBV.

ANOVA Results:

	Sum of Squares	Mean Square	F-stats	p-value	np2
Gender	0.021	0.021	8.03	0.005	0.054
Visit	0.007	0.007	93.31	< 0.001	0.397
Interaction	< 0.001	< 0.001	0.62	0.432	0.004

Above table displaces ANOVA summary. By examining the results, there is a significant difference in mean nWBV between genders since the p-value, 0.005, is less than the significance level. The corresponding effect size, np2, suggests that the gender factor explains approximately 5.4% of the variance in nWBV. The within-subject factor, visit, shows a high statistical significance on its effect since the p-value is less than 0.001, suggesting a significant difference in mean nWBV across different visits. Its effect size suggests that "visit" explains about 39.7% of the variance in nWBV, which is relatively high. The interaction effect between gender and visit is not statistically significant since the p-value is much higher than the significance level.

Post Hoc Tests:
By conducting a post hoc test, additional information about pairwise comparison between levels of the variables visit and gender can be found, regarding their influence on the dependent variable nWBV. The comparison between the first and second visits and the comparison between female and males are both statistically significant since the p-values for both of them are less than 0.05, suggesting a significant difference in mean nWBV between the first and second visits and between females and males. The interaction between visit and gender is statistically significant at both the first and second visit since the p-value is 0.004 and 0.01, meaning the relationship between gender and nWBV varies across different visits.

2. nWBV vs. Visit by Group ANOVA:

Null Hypothesis (H0):
There is no significant difference in mean nWBV across different visits.
There is no significant difference in mean nWBV among different dementia status groups.
There is no significant interaction effect between visits and dementia status groups on mean nWBV.
Alternative Hypothesis (H1):
There is a significant difference in mean nWBV across different visits.
There is a significant difference in mean nWBV among different dementia status groups.
There is a significant interaction effect between visits and dementia status groups on mean nWBV.

ANOVA Results:

	Sum of Squares	Mean Square	F-stats	p-value	np2
Group	0.034	0.017	6.71	0.002	0.087
Visit	0.007	0.007	94.25	< 0.001	0.401
Interaction	< 0.001	< 0.001	1.53	0.219	0.021

Above table displaces ANOVA summary. By examining the results, there is a significant difference in mean nWBV among different dementia status groups since the p-value, 0.002, is less than the significance level. The corresponding effect size suggests that the gender factor explains approximately 8.7% of the variance in nWBV. The within-subject factor, visit, also shows a high statistical significance on its effect since the p-value is less than 0.001, which is identical to the first ANOVA test. Its effect size suggests that "visit" explains about 40.1% of the variance in nWBV, which is relatively high. The interaction effect between gender and visit is not statistically significant since the p-value is much higher than the significance level.

Post Hoc Tests:

By conducting a post hoc test, additional information about pairwise comparison between levels of the variables visit and dementia status groups can be found, regarding their influence on the dependent variable nWBV. Same as previous ANOVA, the comparison between the first and second visits is statistically significant since the p-values is less than 0.001. The pairwise t-test comparing demented and nondemented groups is statistically significant with a p-value less than 0.001, suggesting a significant difference in mean nWBV between these two groups. The interaction between visit and dementia status groups is statistically significant at both the first and second visit between demented and nondemented groups since both p-values are less than 0.001. The effect sizes are -0.59 and -0.66, suggesting a moderate effect, with demented group having lower nWBV compared to the nondemented group during both the first and second visit.

Checking model diagnostics:

Sphericity Assumption:

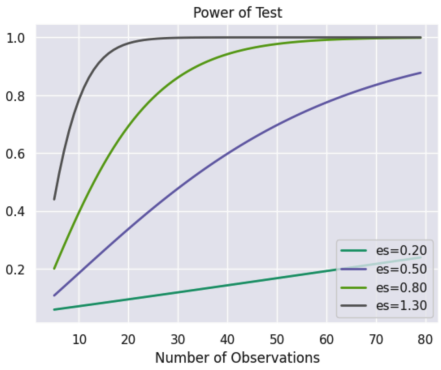
The Mauchly's test of sphericity has been conducted to check whether the assumption of sphericity holds for within-subjects factor, visit. The sphericity assumption checks if the variance of the differences between all possible pairs are equal under within-subject conditions. The p-value associated with the test result is 1.0, indicating a failure to reject the null hypothesis, which means we do not have evidence to suggest that the assumption of sphericity is violated. Hence the data meet the assumption of sphericity.

Normality Assumption:

The Shapiro-Wilk test has been conducted to assess whether the distribution of the dependent variable, nWBV, within each level of the within-subject factor, visit, follows a normal distribution. For the first visit, the test statistic is approximately 0.990, with a corresponding p-value about 0.372; the second visit has a similar test statistic, which is about 0.990, with a corresponding p-value about 0.367. Both p-values are much greater than the significance level, suggesting we do not have sufficient evidence to reject the null hypothesis of normality for both visits. Hence the normality assumption was met as well.

Statistical power analysis:

A theoretical experiment with power = 0.91, alpha = 0.05, and effect size = 0.7 have been conducted. The calculated sample size indicates the number of participants needed in each group to achieve above statistics in a two-sample independent t-test, which is approximately 46 (rounding up).



Power curves:

In this power analysis plot, the x-axis represents the sample sizes ranging from 5 to 80 and the y-axis represents the statistical power. This plot shows the statistical power according to different effect sizes (0.20, 0.50, 0.8, 1.30). With a given effect size, larger sample sizes could lead to higher statistical power, which could provide greater confidence in the result of a study. According to the plot, to achieve a power of 0.91 and an effective size 0.7, approximately 46 subjects are needed within a study, which has been calculated above as well.

Conclusion

By examining the findings from the mixed-effect ANOVAs, the results revealed significant main effects for visit times, gender, and dementia status on nWBV. In general, the second visit, male subjects, and dementia group showed a lower mean nWBV when compared to the others. The interaction effect between visit times and gender and between visit times and dementia status groups on nWBV were not statistically significant, suggesting that the relationship between nWBV and visit times does not differ significantly between gender and among dementia status groups. The study result implies that nWBV may exhibit change over time, and individuals with a lower volume may be more likely diagnosed with dementia. Across genders, females tend to have a higher nWBV than males. However, the study focused on specific subjects, and it did not take individual differences into consideration, hence it may lack generalization. Future research could explore additional factors influencing nWBV to gain a deeper understanding of nWBV and dementia.